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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,333	03/05/2002	Robert B. Dickson	P 0280655	4097

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 08/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/936,333	DICKSON ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *15,16,18,19 and 34-36* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3,15,16,18,19 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 15, 16, 18, 19, and 34-36 are pending and under consideration. In the prior action, mailed on January 27, 2005, claims 1-33 were pending, with claims 1-14 and 20-33 withdrawn as to non-elected inventions, and claims 15-19 under consideration and rejected. In the Response of May 27, 2005, the Applicant amended claims 15, 16, 18, and 19; cancelled claims 1-14, 17, and 20-33; and added new claims 34-36.

Priority

2. **(New Objection)** Applicants claim for priority to prior international application PCT/US00/06111 is noted.

The Applicant has amended the priority statement in the application such that it no longer reflects the status of the present application as a national stage entry of the indicated PCT application. 37 CR 1.78 (a) (2) requires that the reference to an earlier filed application to which priority is being claimed include the relationship between the U.S. application and the application to which priority is claimed, if the earlier application is either an earlier nonprovisional or international application. In the instant case, the earlier application is an international application. The reference to this application should therefore indicate the status of the present application as a national stage application of the international application.

Appropriate correction is required.

Specification

3. **(Prior Objections- Withdrawn)** The disclosure was objected to because of the following informalities: On page 10, line 10 as amended on November 23, 2004, the specification refers to the cDNA sequence of SEQ ID NO: 5. However, SEQ ID NO: 5 is a protein sequence. It is therefore unclear what is being referred to.

On page 22, lines 1-2, the application describes an epitope as a portion of an antigen molecule to which an antibody or an "immunogenic fragment thereof" binds. It was suggested that the phrase be substituted with the phrase "immunologically reactive fragments" as used on page 38 of the application.

In view of the amendments to the application, the objections are withdrawn.

4. **(Prior Objection- Withdrawn)** The specification was objected to as failing to provide proper antecedent basis for the limitation in claim 17 specifying the domain at positions 481-683 of the matriptase protein. In view of the cancellation of claim 17, the objection is withdrawn.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. **(Prior Rejection- Withdrawn)** Claims 15-19 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite because it was not clear if the "immunogenic fragments" of antibodies were intended to describe "immunogenic fragments," or meant to claim "immunologically reactive fragments," as a reading of the application (esp., page 38) and the

substance of the claims would indicate. In view of the amendment of the claims to read on immunogenically reactive fragments, the rejection is withdrawn.

7. **(Prior Rejection- Withdrawn)** Claim 17 was rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In view of the cancellation of the claim, the rejection is withdrawn.

8. **(Prior Rejection- Withdrawn)** Claims 17-20 were rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Each of these claims recites the limitation "the antibody of Claim 14." There is insufficient antecedent basis for this limitation in the claims because there is no antibody identified in claim 14. In view of the cancellation of claims 17 and 20, and the amendment of claims 18 and 19, the rejection is withdrawn.

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. **(Prior Rejection- Withdrawn)** Claim 16 was rejected under 35 U.S.C. 112, first paragraph, as having insufficient written description support for antibodies that bind to any matriptase, including both antibodies that bind to the human matriptase of SEQ ID NOs: 5 and 27, or to related proteins from other species The Applicant has amended the claims such that it

now reads on antibodies against human matriptase. In view of this amendment to the claims, the rejection is withdrawn.

11. **(Prior Rejection- Withdrawn)** Claim 17 was rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. In view of the cancellation of the claim, the rejection is withdrawn.

12. **(New Rejection- Necessitated by Amendment)** Claims 15 and 19 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The claims have been amended to read on specific antibodies; those referred to as M32, M69, and M19. Thus, these antibodies are required to practice the claimed invention. As a required element, it must be known and readily available to the public or obtainable by a repeatable method set forth in the specification, or otherwise readily available to the public. If it is not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of a hybridoma cell producing these monoclonal antibodies. See 37 CFR 1.802. One cannot practice the claimed invention without the identified antibodies because the claims are drawn to these specific antibodies, and the production of antibodies through the disclosed methods is likely to result in the production of antibodies other than these particularly claimed antibodies (see e.g. App., page 90, lines 7-14), and because absent having the specifically claimed antibodies present for comparison or sequencing, those in the art would not be able to determine if they were in possession of the correct antibodies. Therefore, access to them is required to practice the invention.

Deposit of hybridoma cells in a recognized deposit facility would satisfy the enablement requirements of 35 U.S.C. 112, because the strains would be readily available to the public to practice the invention claimed, see 37 CFR 1.801- 37 CFR 1.809.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808.

If a deposit is not made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made at an acceptable depository and that the following criteria have been met:

(a) during the pendency of this application, access to the invention will be afforded to one determined by the Commissioner to be entitled thereto;

(b) all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained for a term of at least thirty (30) years and at least five (5) years after the most recent request for the furnishing of a sample of the deposited material;

(d) a viability statement in accordance with the provisions of 37 CFR 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition the identifying information set forth in 37 CFR 1.809(d) should be added to the specification. See 37 CFR 1.803 - 37 CFR 1.809 for additional explanation of these requirements.

13. **(New Rejection- Necessitated by Amendment)** Claims 16, 18, and 34-36 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are drawn to a genus of antibodies which are described as binding with greater affinity to the two-chain form of matriptase than to the single-chain form.

The following quotation from section 2163 of the Manual of Patent Examination Procedure is a brief discussion of what is required in a specification to satisfy the 35 U.S.C. 112 written description requirement for a generic claim covering several distinct inventions:

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice..., reduction to drawings..., or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus... See Eli Lilly, 119 F.3d at 1568, 43 USPQ2d at 1406.

> A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

Thus, when a claim covers a genus of inventions, the specification must provide written description support for the entire scope of the genus. Support for a genus is generally found where the applicant has provided a number of examples sufficient so that one in the art would recognize from the specification the scope of what is being claimed, although it may also be found by the provision of a functional in combination with structure correlating thereto.

In the present case, the application provides two examples of antibodies that bind to the two-chain human matriptase with greater affinity than to the single chain form: the M123 and M69 antibodies described on pages 89-91. However, while the application discloses that they have isolated these antibodies, they have not provided any means of determining what epitope[s] these antibodies target so as to allow those in the art identify and particular structure that may be targeted which structure would correspond to an epitope present in the two-chain but not in the zymogen form of matriptase.

Further, the teachings regarding the M123 and M69 antibodies provided in the application does not provide sufficient information to demonstrate possession of any antibody that has the required preferential binding. The application provides insufficient written description support for the antibodies themselves in view of the lack of any reproducible means of producing these specific antibodies (i.e., no deposit made or sequence provided). Thus, there is no means by which those in the art could use these antibodies to identify the class to which they belong (e.g. through identifying the target epitope). Further, even if the application did provide adequate description for these two antibodies, the identification of the specific epitopes

bound by these antibodies would provide little description relevant to determining what other epitopes may be targeted to achieve the same function.

Further, claim 36 adds an additional functional limitation requiring the antibody to also bind to the two-chin form of matriptase present in a complex with a Kunitz-type serine protease inhibitor. It is first noted that the application discloses only a single such inhibitor that binds to matriptase- HAI-1 (and fragments thereof). Thus, the application provides only a single species of such inhibitors, and no information identifying other such inhibitors that would also bind to matriptase. Further, while the application indicates that the M123 antibody is also able to perform this function, the association of this antibody with the additional function is insufficient description for any antibody that performs this function for substantially the same reasons as indicated with respect to the preferential binding function previously discussed. I.e., insufficient written description support for the antibody itself, and even in the presence of such, such would be insufficient to describe any antibody that performs both the required functions.

Because the application does not disclose a structure, such as a targeted epitope, that corresponds to the indicated functions, and because the teachings regarding the M123 and M69 antibodies provided in the application does not provide sufficient information to demonstrate possession of any antibody that has the required preferential binding, there is insufficient written description support in the application for any antibody in the identified genus.

Claim Rejections - 35 USC § 102

14. **(Prior Rejection- Withdrawn)** Claims 15 and 16 were rejected under 35 U.S.C. 102(b) as being anticipated by Dickson et al. (U.S. Patent 5,482,848). The claims have been amended to

read on either one of three specific antibodies, or on an antibody that binds preferentially to the two-chain over the zymogen form of human matriptase. Dickson does not teach either of such antibodies. The rejection is therefore withdrawn.

15. **(Prior Rejection- Withdrawn)** Claims 15-18 were rejected under 35 U.S.C. 102(b) as being anticipated by Lin et al. (J Biol Chem 272: 9147-52). In view of the cancellation of claim 17, and the amendments of claims 15 and 16 as described above, the rejection is withdrawn.

16. **(Prior Rejection- Withdrawn)** Claims 15-18 were rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent 6,077,938. The claims have been described above. In view of the cancellation of claim 17, and the amendments of claims 15 and 16 as described above, the rejection is withdrawn.

17. **(Prior Rejection- Withdrawn)** Claims 15, 16, 18, and 19 were rejected under 35 U.S.C. 102(e) as being anticipated by O'Brien et al. (U.S. Patent 5,972,616). The claims have been described above. The claims have been amended as described above. While the reference teaches antibodies to a human matriptase, the reference does not teach or suggest antibodies as per the amended claims. The rejection is therefore withdrawn.

Claim Rejections - 35 USC § 103

18. **(Prior Rejection- Withdrawn)** Claim 18 was rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over U.S. Patent 5,482,848 as applied above. In view of the amendment of claim 16, from which claim 18 depends, the rejection is withdrawn.

19. **(Prior Rejection- Withdrawn)** Claim 19 was rejected under 35 U.S.C. 103(a) as being unpatentable over any of U.S. Patents 5,482,848 or 6,077,938 (collectively- the Dickson patents), or Lin as applied to claims 15 and 16, or 15-18, above and further in view of McKenzie et al. (U.S. Patent 5,084,266) or Huang et al. (U.S. 5,516,637). In view of the amendment of claim 15, from which claim 19 depends, the rejection is withdrawn. None of the patents teach or suggest the particular antibodies identified in amended claim 15.

Double Patenting

20. **(Prior Rejection- Withdrawn)** Claims 15-18 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-9 of U.S. Patent No. 6,077,938. Because the claims of the patent are drawn to an antibody excluded by the amendments to claims 15 and 16, the rejection is withdrawn.

21. **(Prior Rejection- Withdrawn)** Claims 15, 16, and 18 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 4 and 5 of U.S. Patent 5,482,848. Because the patent does not teach or suggest antibodies as required by the present claims as amended, the rejection is withdrawn.

22. **(Prior Rejection- Withdrawn)** Claim 19 was rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim1-9 of U.S. Patent 6,077,938 or of claims 4 and 5 of U.S. Patent No. 5,482,848, further in view of either McKenzie or Huang as described above. This rejection is withdrawn for the reasons indicated above with respect to either claims 1-9 of U.S. Patent No. 6,077,938 or claims 4 and 5 of U.S. Patent 5,482,848.

Conclusion

23. No claims are allowed.

24. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 571-272-0905. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 571-272-0902. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Z. Lucas
Patent Examiner

JAMES HOUSEL 8/8/05
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